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Artificial intelligence-enabled ophthalmoscopy for papilledema: a systematic review protocol

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Abstract

Papilledema is a pathology delineated by the swelling of the optic disc secondary to raised intracranial pressure (ICP). Diagnosis by ophthalmoscopy can be useful in the timely stratification of further investigations, such as magnetic resonance imaging or computed tomography to rule out pathologies associated with raised ICP. In resource-limited settings, in particular, access to trained specialists or radiological imaging may not always be readily available, and accurate fundoscopy-based identification of papilledema could be a useful tool for triage and escalation to tertiary care centres. Artificial intelligence (AI) has seen a rise in neuro-ophthalmology research in recent years, but there are many barriers to the translation of AI to clinical practice. The objective of this systematic review is to garner and present a comprehensive overview of the existing evidence on the application of AI in ophthalmoscopy for papilledema, and to provide a valuable perspective on this emerging field that sits at the intersection of clinical medicine and computer science, highlighting possible avenues for future research in this domain.

Keywords: global health, machine learning, neurosurgery, ophthalmoscopy, papilledema, raised intracranial pressure

Highlights

Papilledema is a condition characterised by the swelling of the optic disc caused by increased intracranial pressure. In low-resource settings where access to specialist imaging is limited, identifying papilledema with accuracy by the bedside using machine learning methods could potentially serve as a tool for triaging when raised intracranial pressure is suspected and urgent surgical–medical intervention may be required. Our systematic review will use a novel rubric for critical appraisal of ML studies, with a focus on medical image analysis and its clinical application.

Introduction

Papilledema is a condition characterised by the swelling of the optic disc caused by increased intracranial pressure (ICP). There are several underlying factors that may lead to elevated ICP, such as space-occupying lesions, brain injury, meningitis, idiopathic intracranial hypertension, spinal cord lesions, cerebral haemorrhage, hydrocephalus, cranial anomalies, or conditions that impair cerebral sinus drainage[1].

The Frisen staging scheme categorises the stages of papilledema seen through ophthalmoscopy on a scale of 0–5 based on the degree of blurring and its impact on nearby vasculature[2]. In later stages, it can be a threat to vision. Timely detection is crucial for identifying the cause and avoiding complications.

Although papilledema is typically symmetrical and bilateral, it is of note that it may be asymmetrical or unilateral in up to 10% of the population[3]. Features of papilledema can be identified with ophthalmoscopy; however, a thorough clinical history, examination, and specialist imaging are often required to identify its cause. It can also be challenging to distinguish papilledema from its mimics, such as optic nerve head drusens, congenital abnormalities, tumours, and hamartomas, using ophthalmoscopy alone[4]. A variety of other ophthalmological tests, such as optical coherence tomography, ultrasonography, and intravenous fluorescein angiography, are often required to distinguish papilledema from its mimics[4]. Depending on clinical suspicion of the aetiology of the papilledema, magnetic resonance imaging (MRI) or computed tomography (CT) may be used to further investigate potential causes for raised ICP.

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However, in environments with limited resources, access to optical CT or complementary brain imaging may not always be possible. Additionally, ophthalmoscopy might not be consistently available, and screening could be performed by non-medical staff. The interpretation of fundoscopic images can be influenced by factors such as the setting, clinical context (acute vs. non-acute), method, expertise, and the self-assurance of the individual performing the task.

In the field of neuro-ophthalmology, artificial intelligence (AI) has shown great promise in detecting both structural and functional disorders of the optic nerve[5], though it remains in its infancy as an area of research. Despite its potential, there are still challenges that need to be addressed before its widespread clinical implementation. Issues such as lack of external validation for some algorithms, limited datasets, small sample sizes for modelling, and discrepancies in image quality between real-life datasets and AI models have contributed to decreased accuracy. However, with continued research and development, these challenges can be overcome.

The EyeVu Consortium

The EyeVu Consortium is an international collaboration of over 30 medical, engineering, and neuroscience students and junior medical trainees from multiple countries, including Nigeria, Zambia, the Democratic Republic of the Congo, Libya, Malta, Peru, Syria, Australia, Turkey, Italy, and the United Kingdom. The consortium was established through the NIHR Global Health Research Group on Acquired Brain and Spine Injuries (ABSI), which is focused on advancing global neurotrauma care through four key research themes: Mapping Care, Understanding Care, Generating and Implementing Innovation, and Capacity Building. This systematic review will establish a literary cornerstone for the consortium's future research initiatives, identifying key gaps and opportunities for innovation.

Aim and objectives

The aim of this systematic review is to provide a comprehensive overview of the current state of evidence regarding the use of AI in ophthalmoscopy for the diagnosis of papilledema. By collating both technical and clinical information, this review seeks to offer insights into this novel intersection of clinical medicine and computer science and shed light on the potential future directions of research in this field.

In meeting this aim, the systematic review will describe and critique the published literature, answering the following research question(s):

1. What is the current state of research on the use of artificial intelligence in ophthalmoscopy for papilledema screening?
2. What algorithms or neural network architectures have been demonstrated to be efficacious in identifying papilledema from ophthalmoscopy images?
3. What datasets, if any, have been used to train the models? Are these datasets open-source and readily available?

Methods

The proposed systematic review will be conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 guidelines[6]. The study has been registered with PROSPERO (CRD42023413049).

Eligibility criteria

This systematic review will include all machine learning studies that use computational algorithms to identify papilledema from retinal images taken using an ophthalmoscope. Studies published in all languages will be considered, with appropriate translation for those not reported in English. All publication dates are eligible for inclusion. The review will exclude studies with non-human subjects, reviews, commentaries, education papers, conference abstracts, protocols, reports, book chapters and miscellaneous grey literature material, as these are unlikely to contain sufficient detail to comprehensively characterise the use of AI-integrated ophthalmoscopy for suspected papilledema in a clinical setting. However, such literature will be examined and undergo backwards citation searching to identify additional potentially eligible articles.

Participants/population

Retrieved studies will describe both adult and paediatric patients who are suspected to have papilledema. Papilledema is a condition that involves swelling and inflammation of the optic nerve, typically caused by raised ICP.

Concept

The focus of this systematic review is on the use of AI for the screening and diagnosis of papilledema. Studies that explore the use of AI in detecting papilledema using ophthalmoscopy or other photographic imaging techniques will be included.

Context

Studies from all contexts and settings will be considered, including those conducted in clinical or hospital settings, community health clinics and research institutions. The geographical location of the studies will not be a limiting factor. Studies published in any language will be considered, but only those with full-text availability will be included.

A summary of Participants/Population, Concept and Context (PCC) criteria for inclusion is reported in **Table 1**.

Search strategy and information sources

The search strategy will be applied to four key databases: Ovid MEDLINE, Ovid Embase, Clarivate Web of Science and IEEE Xplore, retrieving articles from database inception. An example strategy for Ovid MEDLINE [inclusive of MeSH (Medical Subject Headings) terms] is outlined below (**Table 2**).

Selection of studies

The selection of studies will be carried out in two stages. First, following deduplication, two researchers will independently review the titles and abstracts of all retrieved studies to determine their suitability against predefined inclusion (PCC) criteria. Any potential conflicts will be resolved through discussion with a third reviewer. This process will be facilitated by the online Rayyan.ai collaborative review software. Next, potentially eligible articles will undergo a full-text review; at this stage, reasons for exclusion will be noted in accordance with PRISMA reporting guidelines[6].

Table 1

Inclusion criteria.

Participants/Population	All adult and paediatric patients with suspected papilledema.
Concept	Suspected papilledema by ophthalmoscopy and the application of artificial intelligence for its screening/diagnosis.
Context	All contexts and settings.

Data extraction and charting

Data will be extracted from the manuscripts included in the review by two independent researchers using a data charting proforma residing in a Microsoft Excel database. An initial subset of 10 unique articles will undergo data extraction by each researcher before the researchers reconvene and modify and revise the data charting proforma as required. Any remaining articles will be divided between each researcher for subsequent extraction and charting. Charted data will be appraised by a third reviewer to ensure no salient information is missing and ensure consistency.

Critical appraisal of reports of AI in clinical applications: a novel rubric

While a handful of checklists exist for reporting AI in medical imaging applications, such as the CLAIM Reporting checklist[7], there is a paucity of critical appraisal tools for the assessment of the reporting of clinical applications of AI, particularly in medical image analysis with neurosurgery-themed cases, and with a global scope of application. In our systematic review, we plan to utilise a novel 5-domain rubric, 'SMART', comprising 5 domains: (1) Study design, (2) Management and Handling of data, (3) Algorithm, modes and performance, (4) Real-life clinical implications of the model, and (5) Transparency, accountability, medicolegal and ethical considerations. This rubric will be adapted based on previous works and tools available in reporting and assessing quality in diagnostic and prognostic predictive machine learning studies.

Data synthesis and analysis

The extracted data will be presented in both a tabular and narrative format, corresponding to the columns of the data charting proforma. Within the narrative, findings will be summarised in descriptive form pertaining to: study designs adopted (including but not limited to: retrospective or prospective, study setting inclusive of human development index, population demographics, sample or dataset description, representation or diversity within the dataset, and the identification of clinical need or purpose), data management (including but not limited to: method of data acquisition, data storage practices, data sampling, structure and features, representation or diversity within the dataset, data standardisation and interoperability, data pre-processing techniques, the handling of missing data, outliers or other inconsistencies, augmentation techniques, and any descriptive statistics employed), algorithms, models and performance (including but not limited to: algorithm utilised, the reporting of ground truth, hardware used, frameworks, programming languages, packages or libraries used, details of the of selection training, test and validation datasets, model validation and calibration, performance metrics, model calibration, parameter estimates and the selection of hyperparameters, model interpretability or clinical intelligibility, and efforts to make the model open-access), real-life clinical implications of the model (including, but not limited to: description of the model's integration and complement with existing clinical workflows, the model's efficacy in improving patient care or outcomes, transferability to new clinical applications, pathologies or clinical settings, and where relevant, clinical studies conducted that implement the model), and lastly, wider considerations discussed in the model's clinical application (including, but not limited to: a discussion of the algorithm's bias and fairness, reproducibility and transparency of methods, a description or deliberation of the model's potential to cause harm, and any allusion to possible wider ethical, legal or social concerns of the model's use).

Table 2

Ovid MEDLINE search strategy.

Terms pertaining to artificial intelligence or their subsets (machine learning, deep learning)	1. exp Artificial Intelligence/ 2. algorithm*.mp 3. deep learning.mp 4. machine learning.mp 5. artificial intelligen*.mp 6. exp Algorithms/
Terms pertaining to papilledema or other associated descriptors	7. exp Papilledema/ 8. optic nerve swelling.mp 9. optic disc swelling.mp 10. papilledem*.mp
Boolean operators for search term combination	11. 1 OR 2 OR 3 OR 4 OR 5 OR 6 12. 7 OR 8 OR 9 OR 10 13. 11 AND 12

Dissemination

The manuscript arising from this review will be published in a peer-reviewed journal. Additionally, results will be presented at national and international cross-disciplinary conferences to foster future global collaborations and research partnerships exploring the applications of AI in neurosurgical practice.

Discussion

We present a protocol to ascertain a new insight into the application of AI in ophthalmoscopy for papilledema as a correlate of raised ICP. The findings of this systematic review seek to inform further lines of enquiry exploring the development of a novel, AI-integrated smart diagnostic platform for use in resource-limited settings.

Limitations

The proposed review has some limitations. First, due to the relatively new and evolving nature of the field of AI in clinical diagnostics, particularly ophthalmoscopy for suspected papilledema, there may be a limited number of studies available for inclusion. Similarly, we acknowledge that the works formally

published in literature will largely describe successful implementations of AI within ophthalmoscopy and may not necessarily capture less fruitful efforts. Furthermore, we appreciate the possibility that commercially-led use cases of medical AI, such as those reported in white papers or other grey literature, may not be captured by conventional systematic review practices. Nonetheless, the purpose of the review is to systematically identify the use cases of AI in ophthalmoscopy reported in the literature base to date, offering a comprehensive overview of previous and ongoing initiatives conducted to date to aid the future development of an accessible, AI-integrated ophthalmoscopy platform for use in both low-resource and adequate resourced contexts.

Ethical approval

Ethical approval is not required as it is a systematic review of already published studies.

Consent

Informed consent is not required as it is a systematic review of already published studies.

Sources of funding

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Author contribution

L.R. and B.G.S.: contributed equally to the development and writing of the protocol; S.T.: a third reviewer for the inclusion of articles in the study; K.K., A.G.K., P.J.H., and T.B.: reviewed the protocol manuscript; T.B.: supervised the project.

Conflicts of interest disclosure

A.G.K. and P.J.H. are supported by the National Institute for Health Research (NIHR) Cambridge Biomedical Research Centre, Royal College of Surgeons of England, and the NIHR Global Health Research Group on Acquired Brain and Spine Injury. P.J.H. is also supported by an NIHR Research Professorship. K.K. is supported by a NIHR Development and Skills Enhancement Grant. L.R. is a NIHR-funded Academic Clinical Fellow at the University of Leicester. T.B., K.K., and B.G.S are supported by the NIHR Global Health Research Group of Acquired Brain and Spine Injury.

Research registration unique identifying number (UIN)

The study has been registered with PROSPERO (CRD420 23413049).

Guarantor

L.R., B.G.S., and T.B.

Data availability statement

Data sharing is not applicable to this article.

Provenance and peer review

The paper was not invited by the journal.

Author availability statement

We declare that this manuscript is original, has not been published before, and is not currently being considered for publication elsewhere. We confirm that the manuscript has been read and approved by all the named authors. We further confirm that the order of authors listed in the manuscript has been approved by all of us. The contribution of each named author has been described in the 'author disclosure form' attached to the submission.

EyeVu Consortium

The members of the EyeVu Consortium include Abdulhakeem Abubakar Tunde, Abdur Raafay Iqbal, Alex Lawrence, Andrea Cuschieri, Antonia Vogt, Anyela Flor Bruno Peña, Ayda Lazemi, Blendi Bylygbashi, Charles Britton, Chiara Spezzani, Christos Antonopoulos, Daniel Black Boada, Daniel Shao, Dipanshu Gandhi, Ekwegbara Somtochukwu Mitchel, Elena Maerz Engstler, Emmanuel Chileshe Phiri, Geneviève Endalle, Ghina Hussain, Kassim Omar Kassim, Kehinde Alare, Kübra Tamer, Leona Takeuchi, Makinah Haq, Marwa SaedAli Emhemed, Mubarak Mustapha Jolayemi, Muhammad Iqbal Aniq, Nagheli Fernanda Borjas-Calderón, Ngepgou Beckline Tazoah, Nneka Lilian Amakom, O. Joshua Sokan, Olaoluwa Ezekiel Dada, Olobatoke Tunde Ayomide, Oloruntoba Ogunfolaji, Phupha Amornkijja, Razan Eid, Roshen Sidhu, Rushi Patel, Shodip Shrestha, Sruthi Ranganathan, Tangmi Djabo Eric Adrien, Temitayo Ayantayo, Tom Wilkins, Weng Tong Wu, Wesley Barrett, Zafer Utku Ulker.

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